Remarks

At the outset, Applicants wish to thank Examiner Collins for taking the time to meet with Applicants' representative. These remarks are in response to the Final Office Action of December 3, 2003 and the personal interview of May 10, 2004.

In particular, Applicants have amended claims 18 and 23 to require that the offspring or clone carries the claimed DNA. As discussed, this amendment is intended to avoid the rejections under 35 U.S.C. § 112, first and second paragraphs, and 35 U.S.C. § 102 and 103 presented in the Final Office Action of December 3, 2003. Support for this amendment is found in the specification as originally filed, for example, at p.15, line 21 to p. 16, line 1.

Also as discussed, claim 28 has been amended to require a nucleotide having a chain length of at least fifteen nucleotides that is identical to an at least 15-nucleotide fragment of the DNA of SEQ ID NO: 1. As discussed, this amendment is intended to avoid the new matter rejection presented in the Final Office Action. Support for this amendment is found in the specification as originally filed, for example, at p. 12, lines 20 – 25; p. 16, line 21 to p. 17, line 14 and p. 19, lines 31-33.

Furthermore, as discussed, claims 2, 5, 8, 19, 23, and 25 have been amended to clarify that the encoded protein of interest must have Na+/H+ antiporter activity to meet the claim. Support for this amendment is found in the specification as originally filed, for example, at p. 9, lines 28 – 32.

Finally, to expedite prosecution, Applicants have canceled non-elected claims 10-13 and 26 – 27.

Applicants respectfully submit that no new matter has been added.

Pursuant to this amendment, claims 1 – 9, 14 – 25, and 28 are pending in the application. Claims 1, 4, 6, 7, 14 – 17, and 24 were previously indicated as allowable. Accordingly, the present response addresses claims 2 – 3, 5, 8 – 9, 18 – 23, 25, and 28 and the outstanding rejections thereof.

Rejections under 35 U.S.C. § 112, First Paragraph

New Matter:

The Examiner rejected claim 28 under 35 U.S.C. § 112, first paragraph, for containing subject matter not described in the specification (i.e., a new matter rejection). According to the Examiner, the limitation "96% or more" does not find support in the specification as originally filed. To expedite prosecution, Applicants have amended claim 28 to require "identity" (i.e., 100% homology). As discussed in the personal interview, such an amendment finds both implicit and explicit support in the specification as originally filed (see, for example, p. 12, lines 20 – 25; p. 16, line 21 to p. 17, line 14 and p. 19, lines 31 – 33) such that it does not constitute new matter. Thus, Applicants submit that the instant amendment to claim 28 renders this rejection moot and respectfully request reconsideration and withdrawal thereof.

Written Description:

The Examiner rejected claims 2, 3, 5, 8, 9, 19 – 23, 25, and 28 under 35 U.S.C. § 112, first paragraph, as containing subject matter not described in the specification in such as way as to reasonably convey possession of the claimed invention (i.e., a written description rejection).

Applicants respectfully submit that the instant claim amendments render this rejection moot. Specifically, the claims as presently amended involve a genus of nucleotides encoding a narrow range of proteins, particularly defined in terms of specific function and specific structure such that the members of the genus are not expected to be widely variable. Accordingly, one skilled in the art would conclude that Applicants were in possession of the necessary common attributes possessed by the members of the genus.

In the event that the Examiner requires further persuasion, Applicants submit the following comments:

In the Final Office Action as well as the personal interview, Examiner Collins suggested that the hybridizing variants were acceptable, though she still had concern regarding the inclusion of the sequence variants involving a select number of amino acid mutations. Specifically, she noted that the claimed variants were not required to have a specific activity because the preamble recitation that

the DNA "encode an Na+/H+ antiporter" did not limit the variant sequences to those encoding proteins having an Na+/H+ antiporter activity. To expedite prosecution, Applicants have amended claims 2, 5, 8, 19, 23, and 25 to specify that the encoded protein has Na+/H+ antiporter activity. Thus, the claims as presently amended are directed to a genus of nucleotides encoding proteins having a particularly specified function.

In the Final Office Action, the Examiner asserted that the written description rejection was being maintained, despite analogy to Example 14 of the Written Description Guidelines, because the claimed variants, defined in terms of a limited number of sequence modifications, were not equivalent to the variants of Example 14, defined in terms of having at least 95% sequence identity, in that the instant claim language requires that a specific number and type of changes be made to the amino acid sequence of SEQ ID NO: 2. However, central to the issue of written description of genus claims is: does the genus encompass widely variable species? The number of species needed to "represent" a particular genus is directly proportional to the degree of variability of the genus. Accordingly, when reviewing a genus claim, an Examiner must first determine the degree of variability of the genus. When there is substantial variation within the genus, one must describe a wide variety of species to reflect that variation. Conversely, when a genus is not highly variable, only a few (or even one) species need be described. In this case, the USPTO has gone on record establishing that a genus of proteins defined in terms of specific function (i.e., a specified protein activity) and specific structure (i.e., at least 95% homology to a reference protein) is not highly variable. See Training Materials for the Revised Interim Written Description Guidelines published January 5, 2001, particularly Example 14.

Applicants' presently claimed genus of variants is more narrow than that of Example 14, in that the claimed genus only allows for up to 3.7% variation (20 out of 535 amino acids) whereas the genus of Example 14 allows for up to 5% variation. Clearly, if the latter genus is deemed to have a low degree of variability, then the former, more narrow genus must likewise be found to lack substantial variability. In other words, if the USPTO finds proteins that are 95% homologous to have substantial structural similarity, then obviously proteins that are 96.3% homologous must be even more similar from a structural perspective. The fact that one genus defines the structure of its

species in terms of percent homology while the other in terms of number of amino acids mutated is irrelevant; both substantially limit the degree of structural differences allowed. The bottom line is that both claims describe a genus defined in terms of specific function and specific structure such that the members of the genus would be expected to be substantially similar. Since the genus lacks substantial variation, a single species is sufficient to describe and demonstrate possession of the claimed genus. Accordingly, rejection of the instant claims for lack of written description under is in error.

The Examiner further suggested that the rejection was maintained because Applicants had not established that procedures for making the claimed sequence variants of SEQ ID NO: 2 were conventional in the art. Applicants respectfully disagree. Procedures for making variants are indeed well known and conventional in the art. In fact, examples of such procedures are described in Applicants' specification. For example, site-directed mutagenesis techniques may be used to modify the nucleic acid sequence of a particular nucleotide and/or the resulting amino acid sequence of a particular protein. Other mutations may arise in nature. See p. 10, lines 18-23. In any event, as Example 14 bears out, specific guidance as to precise types or points of mutation is not required to demonstrate possession of a claimed genus that lacks substantial variation. Nevertheless, the instant specification indeed provides specific guidance as to which amino acids would be tolerant of mutation. For example, at p. 20, lines 17 – 20, Applicants describe the newly discovered OsNHX1 protein (i.e., the protein of SEQ ID NO: 2) as "highly hydrophobic", composed of 59% hydrophobic amino acids, 22% neutral amino acids, and 19% hydrophilic amino acids. Accordingly, this suggests to one skilled in the art that the preferred substitutions, deletions, insertions and additions will be those that either maintain the balance among hydrophobic, hydrophilic, and neutral amino acids or, alternatively, increase the hydrophobicity. Furthermore, in Figure 3 (sequence alignment figure) and at p. 21, lines 1 – 15, Applicants identify a number of important conserved regions that appear to play a role in Na^+/H^+ antiporter activity. For example, high identity was observed in the transmembrane regions, which are predicted to be involved in ion transport. Also, the motif between amino acids 83 and 92 of SEQ ID NO: 2 was also found to be well conserved and expected to be the binding site for amiloride, an inhibitor of the eukaryotic Na^+/H^+ antiporter. In addition, the sixth and

seventh transmembrane regions were found to be well preserved in eukaryotic Na^+/H^+ antiporter and thus predicted to play an important role in the transport of Na^+ and H^+. This disclosure suggests to one skilled in the art that functional protein variants will be those that involve the substitution, deletion, insertion or addition of amino acids outside of these critical regions. Moreover, one of skill would readily recognize that conserved regions are much less tolerant to mutation than variable regions.

Furthermore, the instant specification sets forth a specific assay for identifying whether a particular variant has Na+/H+ antiporter activity. See p. 9, line 32 – p. 10, line 6. Specifically, the activity of an Na+/H+ antiporter can be detected by the H+ ejection from the biomembranes vesicle due to addition of Na+ as the recovery of fluorescence, for example, by monitoring H+ concentration gradient between isolated biomembranes vesicle formed by H+-ATPase as the fluorescence extinction of acridine orange. See also Fukada et al. (1998) Plant Cell Physiology, 39: 196 – 201, cited at p. 10, lines 4 – 6.

In sum, contrary to the Examiner's suggestion, the present situation is indeed highly analogous to that of Example 14 of the Training Materials. The genus claimed herein is narrowly defined in terms of specific structure and specific function such that one would not expect substantial variation among its members. Furthermore, the instant specification provides both general and specific guidance for making and identifying species encompassed by the genus. Accordingly, one skilled in the art would conclude that Applicants were in possession of the necessary common attributes possessed by members of the genus. Thus, Applicants respectfully submit that the written description rejection of claims 2, 3, 5, 8, 9, 19 – 23, 25, and 28 is in error and, therefore, respectfully request reconsideration and withdrawal thereof.

Enablement:

The Examiner rejected claims 2, 3, 5, 8, 9, 19 – 23, 25, and 28 under 35 U.S.C. § 112, first paragraph, as containing subject matter not described in the specification in such as way as to reasonably enable one to make and use the claimed invention. Again, while the Examiner seems satisfied with the enablement of the hybridizing variants, she continues to object to the sequence

variants involving a select number of amino acid mutations. According to the Examiner, "the specification does not provide sufficient guidance for one skilled in the art to practice the full scope of the claimed invention without undue experimentation". See Final Office Action, bottom of p. 5. Specifically, the Examiner finds that the disclosed working examples combined with the general knowledge in the art regarding making sequence variants does not provide sufficient guidance for making and using the claimed variants because the effect of even a single amino acid substitution, deletion, insertion, or addition on a particular protein's function is unpredictable and because the specification fails to provide specific guidance with respect to which amino acids may be mutated without affecting Na+/H+ antiporter activity. According to the Examiner, absent such guidance, one skilled in the art must resort to trial and error testing in order to distinguish between operative and inoperative embodiments.

As discussed in the personal interview, this rejection appears to stand or fall with the written description rejection. Accordingly, for the reasons given above, Applicants respectfully submit that the instant rejection is also in error and should be withdrawn. Furthermore, it is important to remember that the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, provided it is merely routine. See In re Wands 8 U.S.P.Q. 1400, 1404 (Fed. Cir. 1988). In this case, the "trial and error" testing the Examiner describes is within the parameters of routine experimentation and optimization.

Furthermore, from the Examiner's reasoning, it seems that she would object to "even one" mutation. However, this is clearly in conflict with established USPTO doctrine. As noted previously, when determining enablement, one must answer the question: are the enabled embodiments (i.e., the disclosed working and prophetic examples) representative of the full scope of the claim? As discussed above, the USPTO itself has deemed a single disclosed species to be representative of the claimed genus of variants under similar circumstances. Specifically, one skilled in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions and the high degree of homology set forth in the claims yield structurally similar polypeptides. Accordingly, following the USPTO's own policies and guidelines, it is apparent that an enablement rejection is not proper under these

circumstances. Rather, since the enabled embodiments are "representative" of the full scope of the claim, the full scope of the claim must be found to be enabled.

Furthermore, contrary to the Examiner's suggestion, as discussed above, the instant specification indeed provides both general and specific guidance as to how to make and use the claimed invention, providing not only general guidance as to procedures for making sequence variants (see p. 10, lines 18 – 23) but also provides specific guidance as to which amino acids may be substituted, deleted inserted or added (see Example 2, p. 20, line 10 to p. 21, line 19 as well as Figure 3) and a specific assay for identifying species encompassed by the genus (see p. 9, line 32 to p. 10, line 6).

Accordingly, for the reasons given above, Applicants respectfully submit that the enablement rejection of claims 2, 3, 5, 8, 9, 19 – 23, 25, and 28 is in error and, therefore, respectfully request reconsideration and withdrawal thereof.

Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner separately rejected claims 18 and 23 under 35 U.S.C. § 112, both first and second paragraphs. According to the Examiner, the recitation in claims 18 and 23 of "wherein said transformant plant carries said DNA" was found to lack written description and/or be indefinite because it is unclear whether the phrase "said transformant plant" refers to the parental transformant plant or the transformant plant that is the offspring or clone of the parental transformant plant. The Examiner suggested amending the claims to indicate that the offspring or clone carries the DNA of SEQ ID NO: 1 or a DNA encoding SEQ ID NO: 2 or the DNA encoding the Na+/H+ antiporter.

To expedite prosecution, Applicants have amended claims 18 and 23 in accordance with the Examiner's suggestion. Thus, Applicants respectfully submit that the instant amendments to claims 18 and 23 render these rejections moot and, therefore, respectfully request reconsideration and withdrawal thereof.

Rejections under 35 U.S.C. § 102 and 103

The Examiner rejected claims 18 and 23 under 35 U.S.C. § 102(b) as being anticipated by, or, in the alternative, under 35 U.S.C. § 103 as being obvious over Hiei et al. According to the Examiner, since it is unclear whether the claimed progeny plants comprise the sequence of interest, the claimed invention is anticipated by or obvious in view of any prior art that teaches transgenic plants. In both the Final Office Action and the personal interview, the Examiner indicated that amendment of the claims to indicate that the offspring or clone carries the DNA of interest would overcome this rejection.

To expedite prosecution, Applicants have amended claims 18 and 23 in accordance with the Examiner's suggestion. Thus, Applicants respectfully submit that the instant amendments to claims 18 and 23 render these rejections moot and, therefore, respectfully request reconsideration and withdrawal thereof.

CONCLUSION

Applicants respectfully submit that the claims as amended herein set forth a novel, non-obvious invention. Accordingly, Applicants submit that claims 1-9, 14-25, and 28 as amended herein are in condition for allowance and respectfully petition for an early notice of allowance. However, in the event the Examiner feels that further discussion is merited, she is cordially invited to contact the undersigned.

In view of the foregoing remarks and the amendments above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

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The applicant also invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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